09945325

> d his

(FILE 'HOME' ENTERED AT 14:43:23 ON 11 MAR 2003)

FILE 'REGISTRY' ENTERED AT 14:43:30 ON 11 MAR 2003
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 STRUCTURE UPLOADED
L4 0 S L3
L5 4 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:45:53 ON 11 MAR 2003
L6 11 S L5
S L3

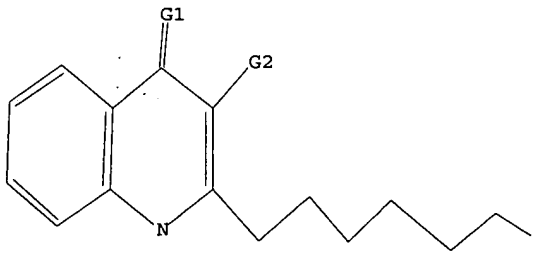
FILE 'REGISTRY' ENTERED AT 14:46:24 ON 11 MAR 2003
L7 0 S L3

FILE 'CAPLUS' ENTERED AT 14:46:26 ON 11 MAR 2003
L8 0 S L7

FILE 'MARPAT' ENTERED AT 14:55:02 ON 11 MAR 2003
L9 0 S L5
L10 45 S L5 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:56:58 ON 11 MAR 2003
L11 44 S L10 NOT L6
L12 0 S L11 AND HEPTYL
L13 6 S L11 AND QUINOLONE
L14 39 S L10 NOT L13
L15 11 S L14 AND HYDROXY
L16 5 S L15 AND 3-HYDROXY

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N
G2 O,N,OH,SH

Structure attributes must be viewed using STN Express query preparation.

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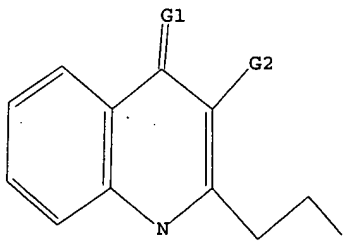
L3 HAS NO ANSWERS
L3 STR



G1 O,S,N
G2 O,N,OH,SH

09945325

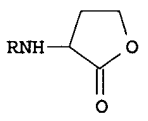
L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2003:42098 CAPLUS
DN 138:90073
TI Synergistic compositions of N-acyl homoserine lactones and 4-quinolones
IN Pritchard, David Idris
PA The University of Nottingham, UK
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003004017	A1	20030116	WO 2002-GB3071	20020703

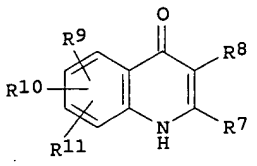
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-16312 A 20010704
OS MARPAT 138:90073
GI



I

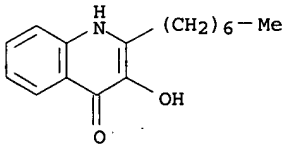


II

AB A compn. having immunosuppressant activity comprises at least one N-acyl homoserine lactone I [R = R3CR1R2CH2CO, R3CH(OH)CH2CO, or R3COCH2CO, where one of R1 and R2 is H and the other is OR4, SR4 or NHR4 (R4 = H or C1-6 alkyl) or R1R2C is keto; R3 = C8-11 hydrocarbyl which is optionally substituted by halo, alkoxy, carboxy, alkoxycarbonyl, or amino groups (R is not 3-oxododecanoyl)] and at least one 4-quinolone II [R7 is an (un)substituted aliph. hydrocarbyl group contg. 1-18 carbon atoms; R8 = H, OH, halo, CHO, CO2H, CONH2 or alkylcarbamoyl; R9-R11 = H, Me, MeO, or halo] or a nontoxic pharmaceutically-acceptable salt. Examples are N-(3-oxoundecanoyl)-L-homoserine lactone and 2-heptyl-3-hydroxy-4(1H)-quinolone, for which syntheses are described. The immunosuppressant activity of the compn. is greater than the sum of the activities of the individual components of the compn. when detd. sep.

IT **108985-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synergistic compns. of N-acyl homoserine lactones and quinolones)

RN 108985-27-9 CAPLUS
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



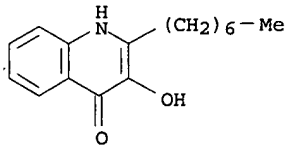
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l6 2-11 bib abs hitstr

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:806904 CAPLUS

09945325

DN 138:53571
TI A bacterial cell to cell signal in the lungs of cystic fibrosis patients
AU Collier, David N.; Anderson, Lisa; McKnight, Susan L.; Noah, Terry L.; Knowles, Michael; Boucher, Richard; Schwab, Ute; Gilligan, Peter; Pesci, Everett C.
CS Brody School of Medicine, Department of Microbiology and Immunology, East Carolina University, Greenville, NC, 27858, USA
SO FEMS Microbiology Letters (2002), 215(1), 41-46
CODEN: FMLED7; ISSN: 0378-1097
PB Elsevier Science B.V.
DT Journal
LA English
AB Pseudomonas aeruginosa is an opportunistic pathogen that is a major cause of mortality in cystic fibrosis (CF) patients. This bacterium has numerous genes controlled by cell to cell signaling, which occurs through a complex circuitry of interconnected regulatory systems. One of the signals is the Pseudomonas Quinolone Signal (PQS), which was identified as 2-heptyl-3-hydroxy-4-quinolone. This intercellular signal controls the expression of multiple virulence factors and is required for virulence in an insect model of P. aeruginosa infection. Previous studies have implied that the intercellular signals of P. aeruginosa are important for human disease, and our goal was to det. whether PQS was produced during human infections. In this report, three types of samples from CF patients infected with P. aeruginosa were analyzed for the presence of PQS. Sputum, bronchoalveolar lavage fluid, and mucopurulent fluid from distal airways of end-stage lungs removed at transplant, all contained PQS, indicating that this cell to cell signal is produced in vivo by P. aeruginosa infecting the lungs of CF patients.
IT **108985-27-9**, 2-Heptyl-3-hydroxy-4-quinolone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas quinolone signal in lungs of cystic fibrosis patients)
RN 108985-27-9 CAPLUS
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



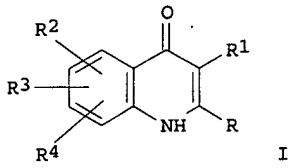
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:465817 CAPLUS
DN 137:33203
TI Substituted-4-quinolones
IN Pritchard, David Idris
PA The University of Nottingham, UK
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047686	A1	20020620	WO 2001-GB5550	20011217
	WO 2002047686	C1	20030109		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002022225	A5	20020624	AU 2002-22225	20011217
PRAI	GB 2000-30729	A	20001216		
	WO 2001-GB5550	W	20011217		

OS MARPAT 137:33203
GI

09945325



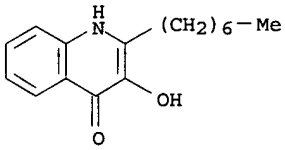
I

AB Substituted-4-quinolones I are claimed, wherein R is a straight or branched chain, satd. or ethylenically-unsatd. aliph. hydrocarbyl group contg. 1 to 18 C atoms which may optionally be substituted by one or more substituent groups selected from halo, 1-6C alkoxy, carboxy, 1-6C alkoxycarbonyl and NR5R6, wherein each of R5 and R6 is independently selected from H and 1-6C alkyl or R5 and R6 together with the N atom to which they are attached form a satd. heterocyclic group selected from piperidino, piperazino and morpholino; R1 is a group selected from H,-OH, halo, -CHO, -CO2H and CONHR7 wherein R7 is H or a 1-6C alkyl; each of R2, R3 and R4 is independently selected form H, -CH3, -OCH3 and halo; or a nontoxic pharmaceutically-acceptable salt thereof, use in the manuf. of a medicament for the treatment of a disease of a living animal body, including a human, which disease is responsive to the activity of an immunosuppressant. The preferred compd. of the formula I is 2-n-heptyl-3-hydroxy-4(1H)-quinolone.

IT **108985-27-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-n-heptyl-3-hydroxy-4(1H)-quinolone as immunosuppressant)

RN 108985-27-9 CAPLUS

CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 2002:171860 CAPLUS

DN 136:215514

TI Novel autoinducer molecules and uses therefor

IN Pesci, Everett C.; Milbank, Jared B. J.; Pearson, James P.; Kende, Andrew S.; Greenberg, Everett Peter; Iglewski, Barbara H.

PA The University of Iowa Research Foundation, USA; University of Rochester; East Carolina University

SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018342	A2	20020307	WO 2001-US27165	20010831
	WO 2002018342	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001086976	A5	20020313	AU 2001-86976	20010831
	US 2002177715	A1	20021128	US 2001-945325	20010831
PRAI	US 2000-229715P	P	20000831		
	WO 2001-US27165	W	20010831		

OS MARPAT 136:215514

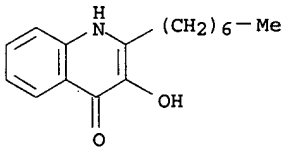
09945325

AB Novel bacterial quinolone signal mols. and, more particularly, Pseudomonas quinolone signal ("PQS") mols., e.g., 2-heptyl-3-hydroxy-4-quinolone, and analogs and derivs. are described,. Therapeutic compns. contg. the mols., and therapeutic methods, methods of for regulating gene expression, methods for identifying modulators of the autoinducer mols., and methods of modulating quorum sensing signaling in bacteria using the compds. of the invention are also described. Thus, 2-Heptyl-3-hydroxy-4-quinolone was isolated from culture broth of Pseudomonas aeruginosa PAO-JP2/pECP39.

IT **108985-27-9DP**, 2-Heptyl-3-hydroxy-4-quinolone, and dervatives of
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(novel Pseudomonas autoinducer mols.)

RN 108985-27-9 CAPLUS

CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 2001:914725 CAPLUS

DN 136:364772

TI A quorum sensing-associated virulence gene of Pseudomonas aeruginosa encodes a LysR-like transcription regulator with a unique self-regulatory mechanism

AU Cao, Hui; Krishnan, Gomathi; Goumnerov, Boyan; Tsongalis, John; Tompkins, Ronald; Rahme, Laurence G.

CS Department of Surgery, Harvard Medical School, Massachusetts General Hopital and Boston Shriners Institute, Boston, MA, 02114, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(25), 14613-14618
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

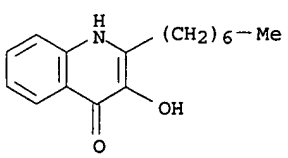
LA English

AB The human opportunistic pathogen Pseudomonas aeruginosa strain PA14 infects both plants and animals. Previously, using plants to screen directly for P. aeruginosa virulence-attenuated mutants, we identified a locus, pho34B12, relevant in mammalian pathogenesis. Here, nonsense point mutations in the two opposing ORFs identified in the pho34B12 locus revealed that one of them, mvfR (multiple virulence factor Regulator), is able to control all of the phenotypes that mutant phoA34B12 displays. Both genetic and biochem. evidence demonstrate that the mvfR gene encodes a LysR-like transcriptional factor that pos. regulates the prodn. of elastase, phospholipase, and of the autoinducers, 3-oxo-dodecanoyl homoserine lactone (PAI 1) and 2-heptyl-3-hydroxy-4-quinolone (PQS), as well as the expression of the phnAB operon, involved in phenazine biosynthesis. We demonstrate that the MvfR protein is membrane-assocd. and acts as a transcriptional activator until cells reach stationary phase, when a unique neg. feedback mechanism is activated to signal the downregulation of the MvfR protein. This work reveals an unprecedented virulence mechanism of P. aeruginosa and identifies a unique indispensable player in the P. aeruginosa quorum-sensing cascade.

IT **108985-27-9**, 2-Heptyl-3-hydroxy-4-quinolone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MvfR controls prodn. of; quorum sensing-assocd. virulence gene of Pseudomonas aeruginosa encodes LysR-like transcription regulator with unique self-regulatory mechanism)

RN 108985-27-9 CAPLUS

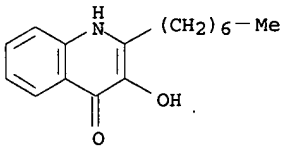
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



09945325

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2001:729021 CAPLUS
DN 136:17770
TI Interference with Pseudomonas quinolone signal synthesis inhibits virulence factor expression by Pseudomonas aeruginosa
AU Calfee, M. Worth; Coleman, James P.; Pesci, Everett C.
CS Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, NC, 27858, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(20), 11633-11637
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB P. aeruginosa is an opportunistic pathogen that controls numerous virulence factors through intercellular signals. This bacterium has 2 quorum-sensing systems (las and rhl), which act through the intercellular signals N-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL) and N-butyryl-L-homoserine lactone (C4-HSL), resp. P. aeruginosa also produces a 3rd intercellular signal that is involved in virulence factor regulation. This signal, 2-heptyl-3-hydroxy-4-quinolone [referred to as the Pseudomonas quinolone signal (PQS)], is a secondary metabolite that is part of the P. aeruginosa quorum-sensing hierarchy. PQS can induce both lasB (encodes LasB elastase) and rhll (encodes the C4-HSL synthase) in P. aeruginosa and is produced maximally during the late stationary phase of growth. Because PQS is an intercellular signal that is part of the quorum-sensing hierarchy and controls multiple virulence factors, basic studies designed to elucidate its biosynthetic pathway were begun. The data strongly suggest that anthranilate is a precursor for PQS. P. aeruginosa converted radiolabeled anthranilate into radioactive PQS, which was bioactive. An anthranilate analog (Me anthranilate) would inhibit the prodn. of PQS. This analog was then shown to have a major neg. effect on elastase prodn. by P. aeruginosa. These data provide evidence that precursors of intercellular signals may provide viable targets for the development of therapeutic treatments that will reduce P. aeruginosa virulence.
IT **108985-27-9**, 2-Heptyl-3-hydroxy-4-quinolone
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(interference with Pseudomonas quinolone signal synthesis inhibits virulence factor expression by Pseudomonas aeruginosa)
RN 108985-27-9 CAPLUS
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

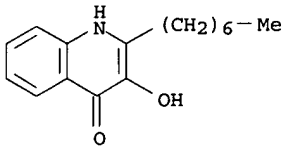
L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2000:296908 CAPLUS
DN 133:218416
TI The Pseudomonas quinolone signal regulates rhl quorum sensing in Pseudomonas aeruginosa
AU McKnight, Susan L.; Iglewski, Barbara H.; Pesci, Everett C.
CS Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, NC, 27858, USA
SO Journal of Bacteriology (2000), 182(10), 2702-2708
CODEN: JOBAAY; ISSN: 0021-9193
PB American Society for Microbiology
DT Journal
LA English
AB The opportunistic pathogen Pseudomonas aeruginosa uses intercellular signals to control the d.-dependent expression of many virulence factors. The las and rhl quorum-sensing systems function, resp., through the autoinducers N-(3-oxododecanoyl)-L-homoserine lactone and N-butyryl-L-homoserine lactone (C4-HSL), which are known to pos. regulate the transcription of the elastase-encoding gene, lasB. Recently, the

authors reported that a second type of intercellular signal is involved in lasB induction. This signal was identified as 2-heptyl-3-hydroxy-4-quinolone and designated the Pseudomonas quinolone signal (PQS). PQS was detd. to be part of the quorum-sensing hierarchy since its prodn. and bioactivity depended on the las and rhl quorum-sensing systems, resp. In order to define the role of PQS in the P. aeruginosa quorum-sensing cascade, lacZ gene fusions were used to det. the effect of PQS on the transcription of the quorum-sensing system genes lasR, lasI, rhlR, and rhlI. The authors found that in P. aeruginosa, PQS caused a major induction of rhlI'-lacZ and had lesser effects on the transcription of lasR'-lacZ and rhlR'-lacZ. The authors also obsd. that the transcription of both rhlI'-lacZ and lasB'-lacZ was cooperatively effected by C4-HSL and PQS. Addnl., the authors present data indicating that PQS was not produced maximally until cultures reached the late stationary phase of growth. Taken together, these results imply that PQS acts as a link between the las and rhl quorum-sensing systems and that this signal is not involved in sensing cell d.

IT **108985-27-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Pseudomonas quinolone signal regulates rhl quorum sensing in Pseudomonas aeruginosa)

RN 108985-27-9 CAPLUS

CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1999:684507 CAPLUS

DN 132:1973

TI Quinolone signaling in the cell-to-cell communication system of Pseudomonas aeruginosa

AU Pesci, Everett C.; Milbank, Jared B. J.; Pearson, James P.; McKnight, Susan; Kende, Andrew S.; Greenberg, E. Peter; Iglewski, Barbara H.

CS Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, NC, 27858, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(20), 11229-11234
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Numerous species of bacteria use an elegant regulatory mechanism known as quorum sensing to control the expression of specific genes in a cell-d. dependent manner. In Gram-neg. bacteria, quorum sensing systems function through a cell-to-cell signal mol. (autoinducer) that consists of a homoserine lactone with a fatty acid side chain. Such is the case in the opportunistic human pathogen Pseudomonas aeruginosa, which contains two quorum sensing systems (las and rhl) that operate via the autoinducers, N-(3-oxododecanoyl)-L-homoserine lactone and N-butyryl-L-homoserine lactone. The study of these signal mols. has shown that they bind to and activate transcriptional activator proteins that specifically induce numerous P. aeruginosa virulence genes. We report here that P. aeruginosa produces another signal mol., 2-heptyl-3-hydroxy-4-quinolone, which has been designated as the Pseudomonas quinolone signal. It was found that this unique cell-to-cell signal controlled the expression of lasB, which encodes for the major virulence factor, LasB elastase. We also show that the synthesis and bioactivity of Pseudomonas quinolone signal were mediated by the P. aeruginosa las and rhl quorum sensing systems, resp. The demonstration that 2-heptyl-3-hydroxy-4-quinolone can function as an intercellular signal sheds light on the role of secondary metabolites and shows that P. aeruginosa cell-to-cell signaling is not restricted to acyl-homoserine lactones.

IT **108985-27-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(quinolone signaling in cell-to-cell communication system of Pseudomonas aeruginosa)

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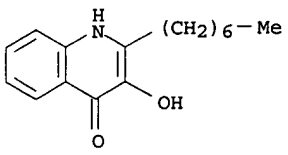
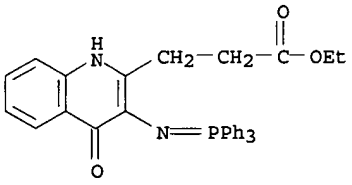
RN 108985-27-9 CAPLUS
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1998:319645 CAPLUS
DN 129:41059
TI Synthesis of 2,3-disubstituted 4-oxoquinolines and 3-substituted fused 4-oxoquinolines
AU Alkhathlan, Hamad Z.; Al-Farhan, Khalid A.
CS Chemistry Department, King Saud University, Riyadh, 11451, Saudi Arabia
SO Heterocycles (1998), 48(4), 641-655
CODEN: HTCYAM; ISSN: 0385-5414
PB Japan Institute of Heterocyclic Chemistry
DT Journal
LA English
AB Seven 2,3-disubstituted 4-oxoquinolines were prepd. via two methods. In the first one 2,3-disubstituted 4-oxoquinolines were prepd. via the condensation of 2-amino-.alpha.-cyanoacetophenone with substituted phthalic anhydrides, while in the second method the fused isoindolo[2,1-.alpha.]quinolines and pyrrolo[1,2-.alpha.]quinolines were first prepd. and then converted to 4-oxoquinolines. X-Ray crystal structure anal. of Et 2-[3-cyano-4-oxo-2-quinolyl]benzoate is reported.
IT **208345-64-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of quinolinone derivs. and fused quinolinone derivs.)
RN 208345-64-6 CAPLUS
CN 2-Quinolinepropanoic acid, 1,4-dihydro-4-oxo-3-[(triphenylphosphoranylidene)amino]-, ethyl ester (9CI) (CA INDEX NAME)

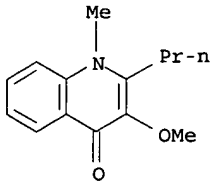


RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

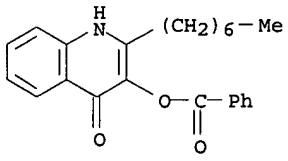
L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1991:118499 CAPLUS
DN 114:118499
TI Isolation, structure, and synthesis of novel 4-quinolinone alkaloids from Esenbeckia leiocarpa
AU Nakatsu, Tetsuo; Johns, Timothy; Kubo, Isao; Milton, Katharine; Sakai, Masami; Chatani, Katsuhiro; Saito, Ken; Yamagiwa, Yoshiro; Kamikawa, Tadao
CS Coll. Nat. Resour., Univ. California, Berkeley, CA, 94720, USA
SO Journal of Natural Products (1990), 53(6), 1508-13
CODEN: JNPRDF; ISSN: 0163-3864
DT Journal
LA English
OS CASREACT 114:118499
AB Two new biocidal quinolinone alkaloids, 3-methoxy-1-methyl-2-propyl-4-quinolone (leiokinine A) and 2(1'-ethylpropyl)-1-methyl-4-quinolone (leiokinine B), were efficiently isolated using reversed-phase recycling HPLC from the leaves of E. leiocarpa. The structures were detd. through spectroscopic data and confirmed by total synthesis. These alkaloids have antifeedant activities against the pink bollworm, Pectinphora gossypiella.
IT **132587-63-4**
RL: BIOL (Biological study)
(from Esenbeckia leiocarpa, isolation and structure of)

09945325

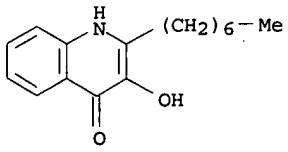
RN 132587-63-4 CAPLUS
CN 4(1H)-Quinolinone, 3-methoxy-1-methyl-2-propyl- (9CI) (CA INDEX NAME)



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1960:86863 CAPLUS
DN 54:86863
OREF 54:16533i,16534a-c
TI Pseudomonas pigments. VII. Isolation of the substance B from the culture of Pseudomonas aeruginosa T 359
AU Takeda, Rokuro
CS Inst. Fermentation, Juso, Osaka
SO Hakko Kogaku Zasshi (1959), 37, 59-63
DT Journal
LA Unavailable
AB A culture (30 l.) of the bacteria in a bouillon medium, pH 8.4 and antibacterial against S. aureus in 180 diln. units, was acidified with HCl to pH 2.0, extd. with ether, the ext. washed with 1% NaHCO3 soln. and then 1% Na2CO3 soln., evapd., the residue heated 1.5 hrs. in 5% HCl, extd. with ether, washed with 1% NaHCO3 and then Na2CO3 solns., and evapd. to give 150 mg. of a substance which was named substance B-A, m. 182-5.degree., [.alpha.]18D 0, with a compn. of C16H21NO2; benzoate, m. 155.degree.. It had weak antibacterial action on gram-pos. bacteria but not on gram-neg. bacteria and molds; it did not antagonize dihydrostreptomycin. From another culture broth were obtained by similar procedures 2 other substances, named B-B and C. The substance B-B m. 122-6.degree. could be sepd. into 8 components by liquid-liquid column chromatography and probably was a mixt. of 4-quinolone derivs., 2-heptyl-4-quinolone being a major component. The substance C, m.p. 130-1.degree., C10H7NO4, was an aromatic compound. The substance B-A was suggested to be 2-heptyl-3-hydroxy-4-quinolone derived from 2-heptyl-4-quinolone.
IT **102559-34-2**, 4(1H)-Quinolone, 2-heptyl-3-hydroxy-, benzoate
108985-27-9, 4(1H)-Quinolone, 2-heptyl-3-hydroxy-
(from Pseudomonas aeruginosa)
RN 102559-34-2 CAPLUS
CN 4(1H)-Quinolone, 2-heptyl-3-hydroxy-, benzoate (6CI) (CA INDEX NAME)



RN 108985-27-9 CAPLUS
CN 4(1H)-Quinolinone, 2-heptyl-3-hydroxy- (9CI) (CA INDEX NAME)

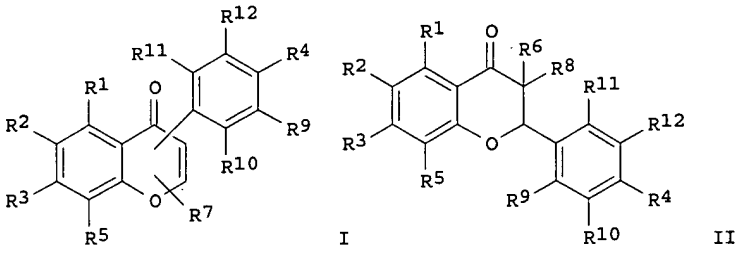


09945325

L16 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2003:35362 CAPLUS
DN **138:89688**
TI Preparation of flavone, isoflavone, and flavanone sulfamates as estrone sulfatase and/or aromatase inhibitors for treatment of breast and endometrial cancers
IN Reed, Michael John; Potter, Barry Victor Lloyd
PA Sterix Limited, UK
SO U.S., 29 pp., Cont.-in-part of U.S. 6,187,766.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6506792	B1	20030114	US 2000-638315	20000814
	WO 9732872	A1	19970912	WO 1997-GB600	19970304
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6011024	A	20000104	US 1998-111927	19980708
	US 6187766	B1	20010213	US 1999-238345	19990127
	AU 726811	B2	20001123	AU 2000-10130	20000106
PRAI	WO 1997-GB600	A2	19970304		
	US 1998-111927	A3	19980708		
	US 1999-238345	A2	19990127		
	GB 1991-18478	A	19910829		
	US 1994-196192	A3	19941227		
	US 1995-458352	A2	19950602		
	GB 1996-4709	A	19960305		
	GB 1996-5725	A	19960319		
	WO 1997-GB444	A2	19970217		
	WO 1997-GB3352	A2	19971204		
	AU 1999-10077	A	19990111		

OS MARPAT 138:89688
GI



AB Title compds. I and II [wherein R1-R12 = independently H, OH, halo, amine, amide, sulfonamine, sulfonamide, any other S-contg. group, alkyl, aryl, ether, ester, or P-contg. group; with the proviso that at least one of R1-R12 = sulfamate] were prepd. as non-steroidal estrone sulfatase and/or aromatase inhibitors. I and II have the advantage of blocking the synthesis of estrone from both androstenediol and E1S and blocking the formation of androstenediol from DHA-S. Hence, invention compds. have considerable therapeutic advantages, particularly for treating breast and endometrial cancers. For example, treatment of 4',5-dihydroxy-7-methoxyflavone with NaH in DMF followed by addn. of sulfamoyl chloride afforded 5-**hydroxy**-7-methoxyflavone-4'-O-sulfamate. The latter inhibited E1-STS activity in MCF-7 breast cancer cells by 88 .+-. 3.1% and 99 .+-. 0.6% at 1 .mu.M and 10 .mu.M, resp., and inhibited aromatase activity in placental microsomes by 82% at 10 .mu.M. Stability studies carried out for selective flavonoid sulfamates under the same conditions as biol. assays established a correlation between sulfamate stability and biol. activity.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS

09945325

AN 2002:171860 CAPLUS
DN **136:215514**
TI Novel autoinducer molecules and uses therefor
IN Pesci, Everett C.; Milbank, Jared B. J.; Pearson, James P.; Kende, Andrew S.; Greenberg, Everett Peter; Iglewski, Barbara H.
PA The University of Iowa Research Foundation, USA; University of Rochester; East Carolina University
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018342	A2	20020307	WO 2001-US27165	20010831
	WO 2002018342	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001086976	A5	20020313	AU 2001-86976	20010831
	US 2002177715	A1	20021128	US 2001-945325	20010831
PRAI	US 2000-229715P	P	20000831		
	WO 2001-US27165	W	20010831		

OS MARPAT 136:215514
AB Novel bacterial quinolone signal mols. and, more particularly, Pseudomonas quinolone signal ("PQS") mols., e.g., 2-heptyl-3-**hydroxy**-4-quinolone, and analogs and derivs. are described,. Therapeutic compns. contg. the mols., and therapeutic methods, methods of for regulating gene expression, methods for identifying modulators of the autoinducer mols., and methods of modulating quorum sensing signaling in bacteria using the compds. of the invention are also described. Thus, 2-Heptyl-3-**hydroxy**-4-quinolone was isolated from culture broth of Pseudomonas aeruginosa PAO-JP2/pECP39.

L16 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2001:798220 CAPLUS
DN **135:344472**
TI Preparation of 6-(5-oxazolyl)-4(1H)-quinolinones as inhibitors of IMPDH enzyme
IN Iwanowicz, Edwin J.; Watterson, Scott H.; Dhar, T. G. Murali; Pitts, William J.; Gu, Henry H.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001081340	A2	20011101	WO 2001-US12900	20010419
	WO 2001081340	A3	20020523		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276739	A2	20030122	EP 2001-928708	20010419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002040022	A1	20020404	US 2001-840503	20010423
PRAI	US 2000-199420P	P	20000424		
	WO 2001-US12900	W	20010419		

OS MARPAT 135:344472
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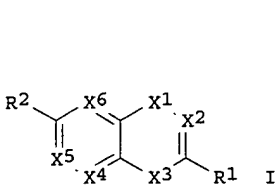

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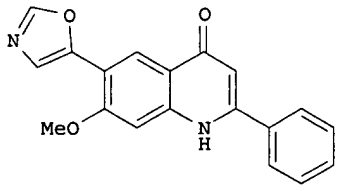


II

AB Title compds. I [wherein X1 = CO, SO, or SO2; X2 = CR3 or N; X3 = NH, O, or S; X4 = CR4 or N; X5 = CR5 or N; X6 = CR6 or N] were prepd. were prepd. as inosine monophosphate dehydrogenase (IMPDH) enzyme inhibitors. For example, acetalization of 4-nitro-2-methoxytoluene with AcOH (51%), redn. to the aldehyde (91%), and cycloaddn. with (p-tolylsulfonyl)methyl isocyanate gave 5-(4-nitro-2-methoxyphenyl)oxazole (84%), which was reduced to the amine (95%). Alkylation with Et benzoylacetate and cyclization afforded the 6-(5-oxazolyl)-4(1H)-quinolinone II. Thus, I are useful as therapeutic agents for IMPDH-assocd. disorders, such as allograft rejection (no data).

L16 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2000:277960 CAPLUS
DN **132:308661**
TI Preparation of (substituted)acyl dipeptidyl inhibitors of the ice/ced-3 family of cysteine proteases
IN Karanewsky, Donald S.; Kalish, Vincent J.; Robinson, Edward D.; Ullman, Brett R.
PA Idun Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000023421	A1	20000427	WO 1999-US24756	19991022
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6242422	B1	20010605	US 1998-177546	19981022
EP 1123272	A1	20010816	EP 1999-970657	19991022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002527504	T2	20020827	JP 2000-577149	19991022
US 2002091089	A1	20020711	US 2001-836442	20010416
NO 2001001968	A	20010619	NO 2001-1968	20010420
PRAI US 1998-177546	A	19981022		
WO 1999-US24756	W	19991022		

OS MARPAT 132:308661
AB Compds. of formula R1X(CH2)nCHR2CO-A-NHCH[(CH2)qCO2R3]CO-B [A is a natural or unnatural amino acid; B = H, D, alkyl, cycloalkyl, (un)substituted Ph or naphthyl, 2-benzoxazolyl, halomethyl, (CH2)mcycloalkyl, (CH2)m(1- or 2-naphthyl), substituted 2-oxazolyl, (un)substituted (CH2)mphenyl, CH2OCO(aryl), or CH2OCO(heteroaryl), etc.; X = CH2, CO, O, S, NH, CONH, CH2OCONH; R1 = (un)substituted Ph, naphthyl, or heteroaryl; R2 = H, alkyl, cycloalkyl, (un)substituted Ph, (CH2)mNH2, (un)substituted (CH2)mphenyl, (CH2)mcycloalkyl, (CH2)mheteroaryl, etc.; R3 = H, alkyl, cycloalkyl, (cycloalkyl)alkyl, (un)substituted phenylalkyl; m = 1-4, n = 0-2; q = 1-2] or their pharmaceutically acceptable salts were prepd. as inhibitors of ICE/ced-3 family of cysteine proteases (ICE = interleukin-1.beta. converting enzyme). Thus, coupling of (1-naphthylamino)acetic acid with (3S)-3-(leucinylamino)-4-oxobutanoic acid tert-Bu ester semicarbazone (prepn. given) followed by deprotection of the resulting intermediate with TFA, and treatment with a 3:1:1 soln. of MeOH/AcOH/37% HCHO afforded (3S)-3-[[N-((1-naphthylamino)acetyl)leucinyl]amino]-4-oxobutanoic acid which showed IC50 = 0.033 .mu.M for mICE, 0.013 .mu.M for CPP32, and 0.037 .mu.M for MCH-2 enzyme assays, resp. The invention is also directed to pharmaceutical compns. contg. these compds., as well as the use of such compns. in the treatment of patients suffering inflammatory, autoimmune and neurodegenerative diseases, for the prevention of ischemic injury, and

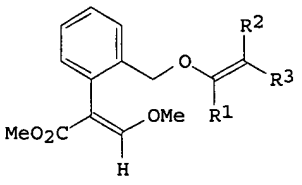
for the preservation of organs that are to undergo a transplantation procedure.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1994:482723 CAPLUS
DN **121:82723**
TI Benzyl enol ethers and their use as plant-protective agents
IN Wingert, Horst; Sauter, Hubert; Benoit, Remy; Roehl, Franz; Ammerman, Eberhard; Lorenz, Gisela
PA BASF A.-G., Germany
SO Eur. Pat. Appl., 123 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 567828	A2	19931103	EP 1993-105924	19930413
	EP 567828	A3	19940105		
	EP 567828	B1	19960124		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	IL 105357	A1	19970713	IL 1993-105357	19930409
	AT 133405	E	19960215	AT 1993-105924	19930413
	ES 2083217	T3	19960401	ES 1993-105924	19930413
	CA 2094359	AA	19931031	CA 1993-2094359	19930419
	JP 06080621	A2	19940322	JP 1993-100774	19930427
	AU 9338227	A1	19931104	AU 1993-38227	19930429
	AU 658291	B2	19950406		
	HU 64176	A2	19931228	HU 1993-1255	19930429
	HU 213728	B	19970929		
PRAI	DE 1992-4214189		19920430		

OS MARPAT 121:82723
GI



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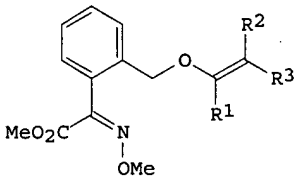

II

AB The title compds. are claimed. More narrowly defined title compds. are the [(alkoxymethylene)(alkoxycarbonyl)methyl]benzyl enol ethers I (R1-R3 = H, cyano, alkyl, etc.). The claimed compds. are agrochem. fungicides. More narrowly defined title compds. are also [(alkoxyimino)(alkoxycarbonyl)methyl]benzyl enol ethers II (same R1-R3).

09945325

13 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1997:238338 CAPLUS
DN **126:225228**
TI Preparation of **quinolone** sulfonimides having leukotriene-antagonistic action
IN Alvarez Domingo, Mercedes; Mauleon Casellas, David; Garcia Perez, Maria Luisa; Fos Torro, Maria De Los Desamparados; Griera Farres, Rosa
PA Laboratorios Menarini S.A., Spain; Alvarez Domingo, Mercedes; Mauleon Casellas, David; Garcia Perez, Maria Luisa; Fos Torro, Maria De Los Desamparados; Griera Farres, Rosa
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9705114	A1	19970213	WO 1996-EP3168	19960718
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
	ES 2108641	A1	19971216	ES 1995-1537	19950731
	ES 2108641	B1	19980816		
	AU 9666576	A1	19970226	AU 1996-66576	19960718
PRAI	ES 1995-1537		19950731		
	WO 1996-EP3168		19960718		

OS MARPAT 126:225228
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = H, C1-4 alkyl, OH, etc.; R2, R3 = H, F, Cl, etc.; R4 = H, F, Cl, MeO; R5 = H, Me; R6 = C1-6 alkyl, cycloalkyl, phenylalkyl; R7 = H, C1-4 alkyl, MeO, etc.; A = O, CH2, NH, NMe], useful as antiinflammatory and antiallergic agents or in the treatment of cardiovascular diseases (no data), were prepd. Thus, reaction of 6-amino-1-[2-methoxy-4-(methoxycarbonyl)benzyl]-1,4-dihydro-4-oxo-quinoline II with cyclopentylacetic acid in the presence of 4-(dimethylamino)pyridine and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride in CH2Cl2 followed by deesterification of the resulting Me ester in MeOH/THF with LiOH in H2O, and reaction of the cyclopentylacetamide III with o-toluenesulfonamide in the presence of 4-(dimethylamino)pyridine and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride in CH2Cl2 afforded the title compd. IV.

L13 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1997:169157 CAPLUS
DN **126:225315**
TI Bicyclic heterocyclic derivatives having .alpha.1-adrenergic and 5HT1A serotonergic activities
IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo
PA Recordati S.A., Chemical and Pharmaceutical Company, Switz.
SO U.S., 84 pp., Cont.-in-part of U.S. 5,474,994.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5605896	A	19970225	US 1994-299188	19940831
	US 5403842	A	19950404	US 1992-888775	19920526
	AU 9336296	A1	19930913	AU 1993-36296	19930223
	RO 112111	B3	19970530	RO 1994-1404	19930223
	PL 175556	B1	19990129	PL 1993-304889	19930223
	RU 2128656	C1	19990410	RU 1994-43324	19930223
	SK 280143	B6	19990910	SK 1994-1007	19930223
	ZA 9301278	A	19931118	ZA 1993-1278	19930224
	LT 3038	B	19940925	LT 1993-354	19930224
	CN 1079738	A	19931222	CN 1993-105852	19930526
	CN 1040434	B	19981028		
	US 5474994	A	19951212	US 1993-67861	19930526
	FI 9403876	A	19940823	FI 1994-3876	19940823

09945325

	NO 9403140	A	19940825	NO 1994-3140	19940825
PRAI	IT 1992-MI408	A	19920225		
	US 1992-888775	A2	19920526		
	US 1993-67861	A2	19930526		
	EP 1993-301264	A	19930222		
	WO 1993-EP420	A	19930223		

OS MARPAT 126:225315
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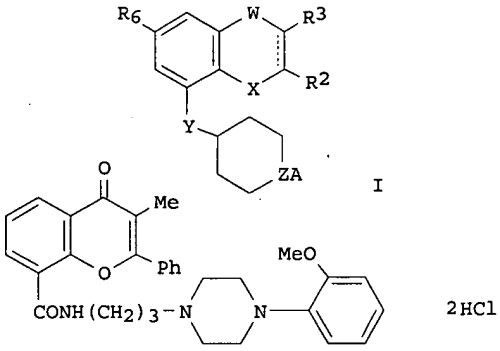
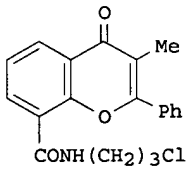


I

2HCl

II



III

AB Bicyclic heterocyclic derivs., such as I [X = N, O, S; W = C(O), C(S), CH(OH), bond; R2 = H, optionally substituted alkyl, alkenyl, alkylnyl, carbocycle, heterocycle; R3 = alkyl, hydroxyalkyl, Ph, OH, alkoxy, alkoxyalkyl; R6 = H, halogen, NO2, NH2, AcNH, mono-, dialkylamino, CN, OH, alkoxy, alkyl; Y = CO, CO2, CONH, CH(OH), CH:CH, CH:CHCO2, CH:CHCONH, CH2NH, CH2NHCO, CH2NHSO2, CH2O, CH2S, NH, NHCO, NHCONH, NHSO2, O, S, SO2NH, CONHO, CSNH, NHCO2, COS, CONH(CH2)m, m = 1-6; Z = N, A = (un)substituted Ph, pyrimidinyl, 1,4-benzodioxan-8-yl, benzopyran-8-yl, benzofuran-7-yl, dihydrobenzopyran-8-yl; Z = CH2N; Z = CH, A = one or two Ph, 4-FC6H4CO, 2-oxo-1-benzimidazolinyl, (CH2)nOA, n = 0-2], and their pharmaceutically acceptable salts useful as .alpha.1-adrenergic and 5HT1A serotonergic agents for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders are described. Thus, benzopyran II was prepd. by heating 1-(2-methoxyphenyl)piperazine with benzopyran III at 180.degree. for 5 h. II had IC50 = 29 nM for .alpha.1-adrenergic receptor binding, IC50 = 9 nM for 5HT1A receptor binding, ED25 = 45 .mu.g/kg i.v. hypotensive effect and ED25 = 1.4 .mu.g/kg in Na-induced urethral contractility assays.

L13 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1996:188920 CAPLUS
DN **124:255246**
TI Luminescent lanthanide chelates and methods of use
IN Selvin, Paul R.; Hearst, John
PA University of California, USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9600901	A1	19960111	WO 1995-US8319	19950629
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5622821	A	19970422	US 1994-269162	19940629
	CA 2193501	AA	19960111	CA 1995-2193501	19950629
	AU 9529567	A1	19960125	AU 1995-29567	19950629
	AU 688928	B2	19980319		

	EP 767912	A1	19970416	EP 1995-925435	19950629
	R: CH, DE, ES, FR, GB, IT, LI, NL, SE				
	JP 10505820	T2	19980609	JP 1995-503466	19950629
	US 5639615	A	19970617	US 1996-762598	19961209
	US 5656433	A	19970812	US 1996-762288	19961209
PRAI	US 1994-269162		19940629		
	WO 1995-US8319		19950629		

OS MARPAT 124:255246

AB The invention provides lanthanide chelates capable of intense luminescence. The chelates comprise a lanthanide chelator covalently joined to a coumarin-like or **quinolone**-like sensitizer. Exemplary sensitizers include 2- or 4-quinolones, 2- or 4-coumarins, or derivs. thereof, e.g., carbostyril 124 (7-amino-4-methyl-2-**quinolone**), coumarin 120 (7-amino-4-methyl-2-coumarin), coumarin 124 (7-amino-4-(trifluoromethyl)-2-coumarin), aminomethyltrimethylpsoralen, etc. The chelates form high affinity complexes with lanthanides, such as terbium or europium, through chelator groups, such as DTPA. The chelates may be coupled to a wide variety of compds. to create specific labels, probes, diagnostic and/or therapeutic reagents, etc. The chelates find particular use in resonance energy transfer between chelate-lanthanide complexes and another luminescent agent, often a fluorescent non-metal based resonance energy acceptor. The methods provide useful information about the structure, conformation, relative location and/or interactions of macromols.

L13 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS

AN 1996:35000 CAPLUS

DN **124:232248**

TI Benzopyran derivatives having affinity for .alpha.1-adrenergic and 5HT1A-serotoninergic receptors

IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo

PA Recordati S.A., Chemical and Pharmaceutical Company, Switz.

SO U.S., 37 pp. Cont.-in-part of U.S. 5,403,842.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5474994	A	19951212	US 1993-67861	19930526
	US 5403842	A	19950404	US 1992-888775	19920526
	EP 558245	A1	19930901	EP 1993-301264	19930222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AU 9336296	A1	19930913	AU 1993-36296	19930223
	RO 112111	B3	19970530	RO 1994-1404	19930223
	PL 175556	B1	19990129	PL 1993-304889	19930223
	SK 280143	B6	19990910	SK 1994-1007	19930223
	CN 1079738	A	19931222	CN 1993-105852	19930526
	CN 1040434	B	19981028		
	FI 9403876	A	19940823	FI 1994-3876	19940823
	NO 9403140	A	19940825	NO 1994-3140	19940825
	US 5605896	A	19970225	US 1994-299188	19940831
PRAI	US 1992-888775	A2	19920526		
	EP 1993-301264	A	19930222		
	IT 1992-MI408	A	19920225		
	WO 1993-EP420	A	19930223		
	US 1993-67861	A2	19930526		

OS MARPAT 124:232248

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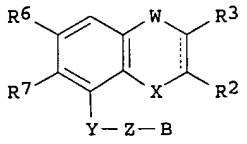
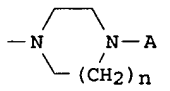
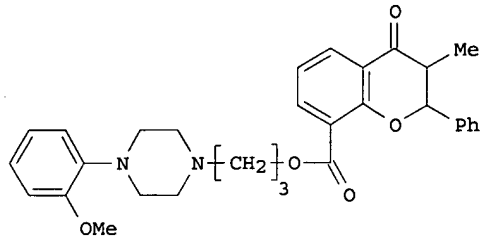


I



II



III

AB This invention provides bicyclic heterocyclic derivs. I wherein the dotted line represents a single or double bond; X represents a nitrogen, oxygen or sulfur atom, or an amino or alkylamino group, a sulfinyl or sulfonyl group; W represents a carbonyl, thiocarbonyl, hydroxymethylene, or a methylene group or a bond; or when X is nitrogen and W is a methine, the fused rings represent a quinoline; R2 represents, e.g, a hydrogen atom or an alkyl, alkenyl, alkynyl, carbocyclic or heterocyclic group, each of which groups may optionally be substituted; or R2 itself represents a trifluoromethyl or an aroyl group; R3 represents a hydrogen atom or an alkyl, hydroxyalkyl, alkyl-O-R4 Ph, hydroxy, or O-R4, wherein R4 represents an alkyl group optionally substituted with an aryl group; R6 represents a hydrogen or halogen atom or a nitro, amino, acylamino, alkylsulfonylamino, alkylamino, dialkylamino, cyano, hydroxy, alkoxy or alkyl group; R7 represents a hydrogen atom or an alkoxy group; Y = e.g., CO, COO, CONH; Z represents a linear or branched chain alkylene group having from 1 to 6 carbon atoms and optionally having one hydroxy substituent; B = e.g., II, n = 1 or 2, A = substituted Ph, 2-pyrimidinyl; and their pharmaceutically acceptable salts useful for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders. The compds. are also useful for binding .alpha.1-adrenergic and 5HT1A serotonergic receptors, in vitro or in vivo. Thus, e.g., esterification of 8-carboxy-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran with 1-(3-chloropropyl)-4-(2-methoxyphenyl)piperazine followed by HCl treatment afforded 8-{3-[4-(2-methoxyphenyl)-1-piperazinyl]propoxycarbonyl}-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran dihydrochloride (III.2HCl) which exhibited IC50's of 20 and 19 nM, resp., for .alpha.1 and 5-HT1A receptor binding. Data were also presented for the effect of I on K+ stimulation of rat bladder strips, and on urethral contractions and blood pressure in dogs.

L13 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1992:214165 CAPLUS
DN **116:214165**
TI Manufacture of biphenylcarbonitriles
IN Roberts, David Anthony; Russell, Simon Thomas; Pittam, John David
PA Imperial Chemical Industries PLC, UK
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 470795	A1	19920212	EP 1991-307184	19910805
EP 470795	B1	19950125		
EP 470795	B2	20010228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9180436	A1	19920213	AU 1991-80436	19910716
AU 646473	B2	19940224		
ZA 9105566	A	19920429	ZA 1991-5566	19910716
CA 2047369	AA	19920210	CA 1991-2047369	19910718
HU 59662	A2	19920629	HU 1991-2481	19910724
HU 207841	B	19930628		
CN 1059516	A	19920318	CN 1991-105206	19910729
FI 9103640	A	19920210	FI 1991-3640	19910730
ES 2067159	T3	19950316	ES 1991-307184	19910805

09945325

	NO 9103086	A	19920210	NO 1991-3086	19910808
	NO 174502	B	19940207		
	NO 174502	C	19940518		
	JP 04253949	A2	19920909	JP 1991-199442	19910808
	JP 3001298	B2	20000124		
	RU 2026285	C1	19950109	RU 1991-5001352	19910808
PRAI	GB 1990-17482	A	19900809		

OS CASREACT 116:214165; MARPAT 116:214165
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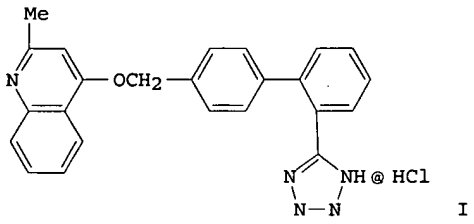

I

AB Biphenylcarbonitriles were prepd. by Pd- or Ni-catalyzed reaction of a B compd. with a nitrile. Thus, (4-methylphenyl)boronic acid reacted with 2-bromobenzonitrile in the presence of PdCl2 and Na2CO3 in H2O-MeOH-toluene to give an 80% yield of 4'-methylbiphenyl-2-carbonitrile. These products can be converted to angiotensin II inhibitors such as tetrazole deriv. I. I showed angiotensin II-antagonist properties in rats with an ED50 of 0.5 mg/kg (i.v.).

L13 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1991:471607 CAPLUS
DN **115:71607**
TI Preparation of arylmethoxyquinolines (tetrazolylbiphenylylmethoxyquinolines) as cardiovascular agents.
IN Roberts, David Anthony; Russell, Simon Thomas; Pearce, Robert James
PA Imperial Chemical Industries PLC, UK
SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 412848	A2	19910213	EP 1990-308855	19900810
	EP 412848	A3	19910410		
	EP 412848	B1	19950118		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2023229	AA	19910212	CA 1990-2023229	19900802
	NO 9003525	A	19910212	NO 1990-3525	19900810
	GB 2234748	A1	19910213	GB 1990-17616	19900810
	GB 2234748	B2	19930630		
	AU 9060955	A1	19910214	AU 1990-60955	19900810
	AU 623546	B2	19920514		
	ZA 9006358	A	19910424	ZA 1990-6358	19900810
	HU 54991	A2	19910429	HU 1990-4961	19900810
	DD 298922	A5	19920319	DD 1990-343371	19900810
	CN 1050187	A	19910327	CN 1990-106923	19900811
	JP 03169863	A2	19910723	JP 1990-214223	19900813
	JP 3010056	B2	20000214		
	US 5444071	A	19950822	US 1993-58825	19930504
PRAI	GB 1989-18402	A	19890811		
	GB 1990-3187	A	19900213		
	US 1990-565764	B1	19900810		

OS MARPAT 115:71607
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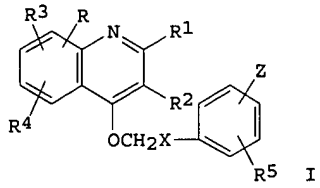

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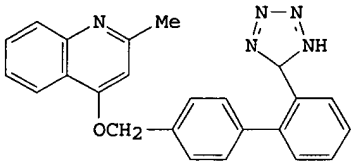

II

AB Title compds. I (R1 = H, alkyl, cycloalkyl, Ph, substituted alkyl; R2 = H, alkyl, cycloalkyl, HO2C, NC, O2N, Ph, phenylalkyl; R3, R4 = H, alkyl, alkoxy, fluoroalkoxy, halo, HO, F3C, NC, O2N, H2O, etc. R3R4 = C1-4 alkylenedioxy attached to adjacent C; R, R5 = H, alkyl, alkoxy, halo, F3C, NC, O2N; X = substituted C6H4, bond; Z = 1-tetrazol-5-yl, etc.) or salts thereof, useful for treatment of hypertension and congestive heart failure, are prepd. 2-Methyl-4-(2-(2-triphenylmethyl-2H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline (prepn. from 2-methyl-4-**quinolone** and the corresponding bromomethylbiphenyl given), dioxane.HCl and H2O were kept for 72 h to give title compd. II.HCl (III). In tests for antagonizing angiotensin II in vitro and in vivo, III showed IC50 1.7 .times. 1--8M, pA2 8.95, and ED50 of 0.5 mg/kg, i.v. In addn. I demonstrated a significant redn. in blood pressure at 50 mg/kg or less, without any overt toxicol. or other unsatd. pharmacol. effects. A large no. of I and intermediates were prepd. Pharmaceutical formulations comprising I are given.